REMARKS

Applicant respectfully requests reconsideration.

Claims 1-15, 18-45 and 96-102 were previously pending in this application. Claims 14, 15, 40-42, 45 and 96-98 were withdrawn.

Claims 1, 12, 39, 44 and 99 have been amended. Claim 1 has been amended to recite "wherein the immunostimulatory nucleic acid comprises a CpG motif which is unmethylated." Support for this amendment can be found in the specification at least on page 11 lines 17-20 and page 14 lines 1-10. Claim 12 has been amended to correct a typographical error. Claims 39 and 44 have been amended to modify the language. Support for these amendments can be found in the specification at least on page 6 lines 11-14, page 25 line 24 to page 26 line 14, page 32 lines 19-28, page 83 lines 4-6, page 83 line 20 to page 84 line 6, page 85 lines 1-2 and page 88 lines 27-29. Claim 99 has been amended to recite "wherein the immunostimulatory nucleic acid is 21-100 nucleotides in length." Support for this amendment can be found in the specification at least on page 11 lines 15-16.

Claims 1-13, 18-39, 43, 44 and 99 are currently under examination, and claims 100-102 are allowed.

No new matter has been added.

Claim Objections

The Examiner objected to claim 21 for being dependent on a rejected claim. Applicant addresses the rejection of claim 1, from which claim 21 depends, below. In view thereof, Applicant believes that claim 1 is in condition for allowance, and thus claim 21 is also.

Reconsideration and withdrawal of this objection is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Enablement

The Examiner maintained the rejection of claims 39 and 44 under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement.

Without conceding the correctness of the rejection, and solely in the interest of expediting prosecution, Applicant has amended claim 39 to recite "wherein the immunostimulatory nucleic acid is provided in an amount effective to stimulate an immune response against an infectious agent". Support for this amendment can be found in the specification at least on page 6 lines 11-14, page 25 line 24 to page 26 line 14, page 32 lines 19-28, page 83 lines 4-6, page 83 line 20 to page 84 line 6, page 85 lines 1-2 and page 88 lines 27-29. Applicant has also amended claim 44 to recite that the infectious agent is herpes simplex virus. Support for this amendment can be found in the claim as originally filed. Applicant notes that, as discussed in greater detail below, the cited references support the ability of CpG nucleic acids to stimulate immune responses against infectious agents, and thus these references support rather than refute the enablement of claims 39 and 44 as now amended.

State of the art and predictability in the art:

Applicant had previously cited US Patents 6,194,388 and 6,207,646 to demonstrate that, as of the filing date of the application, the art was aware that CpG nucleic acids were immunostimulatory. The Examiner acknowledges this point by stating that the cited patents demonstrate that an immune response can be generated by CpG nucleic acids. In addition, claim 1 US Patent 6,207,646 recites *inter alia* "ameliorating an immune system deficiency", which can be the presence of an infectious agent (see claim 2), by administering a CpG immunostimulatory nucleic acid. In granting this patent, the USPTO clearly considered that a broad class of CpG nucleic acids could ameliorate the presence of an infectious agent, even in view of a state of the art that existed at least 7 years prior to the effective filing date of the rejected claims.

Regarding Choi *et al.*, Vaccine 2002, 20:1733-1740 and Gallichan *et al.*, J. Immunol 2001, 166 (5):3451-3457, the Examiner states that Fig. 7 of Gallichan *et al.* shows that CpG nucleic acid administration alone does not "prevent or treat infection." For the record, Applicant notes that the instant specification defines "treat" in part as meaning to "reduce or eliminate an infection or prevent it from becoming worse" (see page 27 lines 17-22) and that Fig. 7 shows a reduction in viral titre upon CpG nucleic acid administration. With respect to claims 39 and 44 as now amended, Fig. 7 further shows immune response induction (resulting in viral titre reduction) upon administration of CpG nucleic acids alone. Moreover, the Examiner acknowledges that the references "illustrate

that CpG nucleic acids were used as adjuvants with rotavirus antigen or herpes simplex virus antigen." Thus, the teachings of Choi *et al.* and Gallichan *et al.* support claims 39 and 44 as now amended.

Regarding Krieg *et al.* (Abstract) Meeting Molecular Approaches to the Control of Infectious Diseases, Sept. 9-Sept. 13, 1996, the Examiner asserts that Krieg *et al.* does not "correlate reduction of infection with treatment of disease symptoms." Applicant notes that claims 39 and 44 as amended recite stimulating an immune response. Krieg *et al.* discloses that mice that were pre-treated with CpG nucleic acids, prior to exposure to an infectious agent, demonstrated an immune response against the infectious agent, as evidenced by reduction in colony formation. Thus Krieg *et al.* provides evidence that CpG nucleic acids are able to stimulate an immune response against an infectious agent.

Regarding Juffermans *et al.* Infect. Immun. 2002, 70(1):147-152, the Examiner asserts that the reference does not "correlate reduction of infection with treatment or prevention of tuberculosis disease." Applicant notes that claims 39 and 44 as now amended do not recite treatment or prevention of disease. Rather these claims recite stimulating an immune response. Juffermans *et al.* discloses that CpG nucleic acid administration to mice, prior to infection with an infectious agent, "resulted in enhanced survival and a reduction in mycobacterial burden in the pulmonary compartment" (see page 150, right column, second paragraph). Juffermans *et al.* discloses the benefits of CpG nucleic acid administration to reduce or eliminate an infection or prevent it from becoming worse. Furthermore Juffermans *et al.* evidences that CpG nucleic acids can stimulate an immune response against an infectious agent, as recited in claims 39 and 44 as now amended.

Regarding Gramzinski *et al.* Infect. Immun. 2001 69:1643-1649, the Examiner acknowledges that the reference teaches that CpG nucleic acids stimulate an immune response but asserts that the reference does not "correlate the immune response generated ... with treatment of a malaria disease." Applicant notes that claims 39 and 44 as now amended do not recite treatment or prevention of disease. Rather these claims as amended recite stimulating an immune response. Gramzinski *et al.* demonstrates that a single dose of a single CpG nucleic acid induced protective immunity against P. yoelli infection. In particular, Table 1 documents that none of the ten mice administered a single dose of CpG nucleic acid 1 or 2 days before P. yoelli infection became

infected whereas all ten of the control mice did. Thus, Gramzinski *et al.* evidences that CpG nucleic acids can stimulate an immune response against an infectious agent, as recited in claims 39 and 44 as now amended.

The Examiner further contends that, since Juffermans *et al.* and Gramzinski *et al.* teach CpG nucleic acid sequences that are different from those of the rejected claims, "one cannot extrapolate" from the results of these references. The Examiner's position is inconsistent. The Examiner has cited Juffermans *et al.* and Gramzinski *et al.* to support the enablement rejection and in doing so apparently considers that their teachings can be extrapolated to the rejected claims. However, when Applicant argues that Juffermans *et al.* and Gramzinski *et al.* actually support rather than rebut enablement, the Examiner states that the reference teachings cannot be extrapolated to the nucleic acids of the rejected claims. The Examiner cannot have it both ways: either the reference is available for all that it teaches or it is not. The Examiner cannot broadly apply a reference and then narrow its value in the context of Applicant's rebuttal.

Regarding Weiner *et al.* J. Leukocyte Biology 2000 68:455-463, the Examiner acknowledges that the reference demonstrates immune response generated using a CpG nucleic acid. As discussed in the previous Office Action response, Weiner *et al.* summarizes the immunostimulatory activity of CpG nucleic acids and, in doing so, actually argues for rather than against predictability in the art. Weiner *et al.* discloses that CpG nucleic acids induce cytokines and activate immune cell subpopulations. Moreover, Weiner *et al.* discloses that CpG nucleic acids provide protection against challenge with an infectious agent (see page 458, left column, fourth paragraph). The claimed nucleic acids possess similar immunostimulatory profiles as those described by Weiner *et al.*, including B and NK cell activation, antibody secretion, IP-10 and IL-10 production, and IFN- α secretion. Weiner *et al.* further teaches a correlation between the in vitro and in vivo immunostimulatory effects observed with CpG nucleic acids (see page 457, right column, third paragraph). When taken as a whole, therefore, the reference supports predictability of immunostimulation using CpG nucleic acids.

Regarding Ballas *et al.* J. Immunology 2001 167:4878-4886, the Examiner asserts that the choice of CpG is critical in "cancer immunotherapy." Applicant notes that the rejected claims are not directed to cancer immunotherapy and therefore the relevance of this reference to these claims is

questionable. Regarding Agrawal *et al.* Trends in Molecular Medicine 2002 8(3):114-120, the Examiner asserts that this reference teaches variability between CpG nucleic acids. Applicant reiterates that the rejected claims relate to nucleic acids that share a 21 nucleotide core consensus sequence and importantly that are demonstrated in the Examples to be immunostimulatory. Any discussion of variability is moot in view of the data presented in the instant specification. Moreover, Agrawal *et al.* is actually a review of the therapeutic uses of CpG nucleic acids, including their use in generating an immune response against specific antigens. Thus the reference supports claims 39 and 44 as now amended.

The Examiner contends that, based on the collection of cited references, one of ordinary skill in the art could not predict whether the claimed nucleic acids would be immunostimulatory. The Examiner's statement completely disregards the specification's experimental demonstration that the claimed nucleic acids are immunostimulatory. One of ordinary skill in the art need not predict such activity as it is explicitly shown in the Examples.

Level of ordinary skill in the art and amount of direction provided by the inventor(s):

The specification discloses the claimed nucleic acids and shows them to be immunostimulatory. The specification also discloses infectious agents. It is within the skill of the ordinary artisan to determine the amount of such nucleic acids that would be effective in stimulating an immune response against an infectious agent whether in vitro or in vivo.

Working examples:

Immune response induction by the claimed nucleic acids, including antigen specific immune response, is demonstrated in the specification. The Examiner acknowledges this. Such immune responses are consistent with immune responses in vivo and in vitro against infectious agents. Thus, the working examples presented in the specification correlate with the scope of rejected claims.

Quantity of experimentation needed to practice the invention:

Claims 39 and 44 as amended recite stimulating an immune response against an infectious agent. The specification teaches the claimed nucleic acids and shows their immunostimulatory activity. The art recognizes that immune responses can be generated against infectious agents. Such immune responses are similar in profile to the immune induction profile of the claimed nucleic

acids. The Examiner acknowledges that the claimed nucleic acids can generate an immune response (see page 8 of the Office Action: "the instant specification demonstrates that the instant nucleic acid induces an immune response..."). Accordingly, the rejected claims can be practiced without undue experimentation and thus they are enabled.

Reconsideration and withdrawal of this rejection is respectfully requested.

Written Description

The Examiner rejected claims 1-13, 18-20, 22-39, 43 and 44 under 35 U.S.C. § 112, first paragraph, for allegedly lacking written description. The Examiner asserts that the claims lack sufficient written description for the recitation in claim 1 of "wherein the C of at least one of the four CpG motifs is unmethylated."

Without conceding the correctness of the rejection, and solely in the interest of expediting prosecution, Applicant has amended claim 1 to recite "wherein the immunostimulatory nucleic acid comprises a CpG motif which is unmethylated." Support for this amendment can be found in the specification at least on page 11 line 17-20 and page 14 lines 1-10. The specification discloses that "[a] CpG nucleic acid is a nucleic acid that comprises the formula 5'$X_1X_2CGX_3X_43$' wherein C is unmethylated..." (page 14 lines 8-10). Claim 1 is therefore sufficiently described in the specification. Claims 2-13, 18-20, 22-39, 43 and 44 depend from claim 1 and incorporate the features of this claim and are also sufficiently described.

Reconsideration and withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claim 99 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite.

The Examiner asserts that "less than 100 nucleotides in length" is unclear. Applicant respectfully disagrees. One of ordinary skill in the art would readily recognize that the claimed oligonucleotides must be at least 21 bases in length (i.e., the length of SEQ ID NO:1). However, in the interest of expediting prosecution, Applicant has amended claim 99 to recite "wherein the

immunostimulatory nucleic acid is 21-100 nucleotides in length." Support for this amendment can be found in the specification at least on page 11 lines 15-16.

Reconsideration and withdrawal of this rejection is respectfully requested.

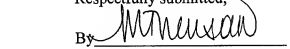
CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Dated: October 30, 2008

Respectfully submitted,

By 

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